

REMARKS

The rejection of Claims 6-8 under the judicially-created doctrine of obviousness-type double patenting over Claims 1-5 of U.S. 6,713,525 (parent patent) in view of U.S. 6,376,571 (Chawla et al), is respectfully traversed. The claims of the parent patent are drawn to the presently-recited urethane(meth)acrylate oligomer. Chawla et al discloses fast curing radiation-curable compositions for coating optical fibers (column 1, lines 10-25). Chawla et al's composition contains a cure speed enhancing radiation-curable monomer or oligomer having at least one functional group capable of polymerization in the presence of radiation being directed connected to a propoxy group (column 4, lines 26-31), wherein the propoxy groups are branched (column 6, lines 59-62). Chawla et al exemplifies, in Examples 1 and 2, a radiation-curable oligomer prepared from hydroxyethylacrylate, polytetramethylene ether glycol and isophoronediiisocyanate, which oligomer is further reacted with an unsaturated monomer containing the above-discussed propoxy group (column 14, line 25ff). The polytetramethylene ether glycol of Chawla et al has been shown in the specification herein to produce inferior results. See Example 6, which is a comparative example, which, as shown in Table 2 herein, has an undesirably high viscosity and a low break elongation. Without the present disclosure as a guide, one skilled in the art would not have employed the particular urethane(meth)acrylate oligomer of the claims of the parent patent to coat an optical fiber. Accordingly, it is respectfully requested that this rejection be withdrawn.

The rejection of Claims 6-8 under 35 U.S.C. § 103(a) as unpatentable over U.S. 6,197,459 (Leach) in view of Chawla et al, is respectfully traversed. Leach discloses a photosensitive resin for use in making a printing plate comprising a polyurethane prepolymer, at least one monomer having at least one (meth)acrylate group, and a photopolymerization initiator, wherein the urethane prepolymer is formed by the reaction of one or more polyether diols, a molecule having at least two isocyanate groups, and a molecule having at least one

hydroxyl group and at least one (meth)acrylate group, wherein the polyether diol component has a level of terminal olefin unsaturation of less than 0.01 meq/gm, and more preferably less than 0.007 meq/gm (column 3, lines 42-54). Preferred polyether diols, and the only one specifically described, are ethylene oxide-propylene oxide copolymers (column 4, lines 8-9). The polyether diols are disclosed as preferably having a number average molecular weight of from about 500 to about 5,000 (column 4, lines 39-41). The viscosity of the photosensitive resin composition is disclosed as preferably between 10,000 cps and 100,000 cps, and most preferably from about 25,000 cps to about 40,000 cps (column 6, lines 7-10).

Chawla et al, in addition to what has been stated above, discloses that their radiation-curable compositions are useful for as printing plate material as well as the above-discussed coated optical fibers.

While Chawla et al's radiation-curable compositions may be disclosed for both making printing plates and coating optical fibers, there is no disclosure or suggestion in Chawla et al that **any** photosensitive resin composition disclosed as a printing plate material would also be useful for coating optical fibers. At best, the Examiner has made out an "obvious to try" case.

"Obvious to try" has long been held not to constitute obviousness. *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988) (**copy enclosed**). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995) (**copy enclosed**).

Claims 9-14 are each separately patentable because the only polyether diols described by Leach are ethylene oxide-propylene oxide copolymers. No polyoxypropylene polyols are described.

In addition, Claim 12 is separately patentable, because Leach's molecular weight range of from 500 to 5,000 corresponds to a hydroxyl value (V_{OH}) of from 224 to 22 mg KOH/mg, as pointed out during the prosecution of the parent application, and as repeated below.

Since a hydroxyl value (V_{OH}) is defined as the number of mg of potassium hydroxide (KOH: MW = 56.11) required to neutralize the acetic acid capable of combining by acetylation with 1 g of sample, the following relationship is generally known to hold between molecular weight (M) and the hydroxyl value (V_{OH}):

$$M = (56.11 \times 1000 \times N) / V_{OH},$$

where N is the number of hydroxyl groups, which is 2 in Leach (see column 5, line 25, of U.S. 6,503,997 (Saito et al), of record, as a reference demonstrating that this relationship is commonly known to the skilled artisan). A molecular weight range of from 500 to 5000 disclosed in Leach, using the above relationship, corresponds to a (V_{OH}) range of from 224 to 22 mg KOH/g. In fact, Leach discloses that this range is preferable; thereby teaching away from a polyol having hydroxyl values (V_{OH}) of greater than 224 and less than 22 mgKOH/g. Therefore, Leach clearly fails to disclose or suggest an oligomer having a hydroxyl value (V_{OH}) of from 17 to 9 mg KOH/g.

In direct contrast, polyols having a hydroxyl value (V_{OH}) of from 17 to 9 mg KOH/mg, when used to form oligomers that are cured, have excellent elongation properties, e.g. flexible, enabling it to be used e.g. coating material; thereby providing excellent follow-up action to a substrate. Further, an oligomer so prepared may have a low glass transition temperature so that the physical properties thereof do not change greatly within the normally used temperature, especially when the Tg of a soft segment is low. Further, it means that the flexibility attributable to the soft segment does not change greatly within the normally used temperature range. Accordingly, a cured structure having the recited oligomer may have a

low Tg and physical properties that may not change readily, which is very important to a coating material.

Claim 15 is separately patentable because Leach describes diols only. Claim 16 is separately patentable because Leach requires a maximum unsaturation of 0.01 meq/gm.

Claim 17 is separately patentable because Leach discloses a minimum viscosity of 10,000 cp.

Since Claims 9-17 are separately patentable, as discussed above, it follows that analogous Claims 18-35 are separately patentable as well.

For all the above reasons, it is respectfully requested that this rejection be withdrawn.

All of the presently-pending claims in this application are now believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Norman F. Oblon



Harris A. Pitlick

Registration No. 38,779

Customer Number

22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/03)
NFO/HAP/cja

In re Johnson and Farnham, 194 USPQ 187 (CCPA 1977)

In re Johnson and Farnham

**(CCPA)
194 USPQ 187**

Decided June 16, 1977

No. 76-643

U.S. Court of Customs and Patent Appeals

Headnotes

PATENTS

1. Claims -- Indefinite -- In general (§ 20.551)

Construction of specification and claims -- By prior art (§ 22.20)

Analysis of 35 U.S.C. 112 second paragraph rejection should begin with determination of whether claims satisfy requirements of second paragraph; first inquiry, therefore, is to determine whether claims set out and circumscribe particular area with reasonable degree of precision and particularity; it is here where definiteness of language employed must be analyzed, not in vacuum, but always in light of teachings of prior art and of particular application disclosure as it would be interpreted by one possessing ordinary level of skill in pertinent art.

2. Claims -- Indefinite -- In general (§ 20.551)

Claims -- Specification must support (§ 20.85)

Undue breadth of claims is not indefiniteness.

3. Construction of specification and claims -- By specification and drawings -- In general (§ 22.251)

Claim language must be read in light of specification as it would be interpreted by one of ordinary skill in art.

4. Claims -- Indefinite -- In general (§ 20.551)

Claims -- Specification must support (§ 20.85)

Pleading and practice in Patent Office -- Rejections (§ 54.7)

Specification -- Sufficiency of disclosure (§ 62.7)

Examiner's rejection premised on general ground that claims are "broader than the express limitation disclosed as defining the invention" and specific grounds that "express disclosure is clearly limited to the sigma value recited in claim 1," raises lack of enablement issue properly arising under first not second paragraph of Section 112.

5. Specification -- In general (§ 62.1)

Specification -- Claims as disclosure (§ 62.3)

It is function of specification, not claims, to set forth "practical limits of operation" of invention; one does not look to claims to find out how to practice invention they define, but to specification.

6. Claims -- Specification must support (§ 20.85)

Construction of specification and claims -- In general (§ 22.01)

Specification -- Sufficiency of disclosure (§ 62.7)

Specification as whole must be considered in determining whether scope of enablement provided by specification is commensurate with scope of claims.

7. Construction of specification and claims -- Broad or narrow -- In general (§ 22.101)

Patent grant -- Intent of patent laws (§ 50.15)

Specification -- Sufficiency of disclosure (§ 62.7)

Claims must adequately protect inventors to provide effective incentives; to demand that first to disclose shall limit his claims to what he has found will work or to materials that meet guidelines specified for "preferred" materials in involved process would not serve constitutional purpose of promoting progress in useful arts.

8. Applications for patent -- Continuing (§ 15.3)

Applicants are entitled to benefit of filing date of parent application that discloses invention of application in manner provided by Section 112, paragraph 1.

9. Claims -- Broad or narrow -- In general (§ 20.201)

Estoppel -- Involving interference (§ 35.20)

It is for inventor to decide what bounds of protection he will seek; it is applicant's right to retreat to otherwise patentable species merely because he erroneously thought he was first with genus when he filed.

10. Specification -- Sufficiency of disclosure (§ 62.7)

Notion that one who fully discloses, and teaches those skilled in art how to make and

Page 188

use genus and numerous species has failed to disclose and teach those skilled in art how to make and use genus minus two species and has thus failed to satisfy Section 112 first paragraph requirement results from hypertechnical application of legalistic prose relating to that provision of statute.

11. Pleading and practice in Patent Office -- In general (§ 54.1)

Specification -- Sufficiency of disclosure (§ 62.7)

While insufficiency under 35 U.S.C. 112 cannot be cured by citing causes for insufficiency, it is not true that factual context out of which question under Section 112 arises is immaterial; specification having described whole invention necessarily described part remaining after

invention of another was excised.

Particular patents -- Polyarylene Polyethers

Johnson and Farnham, Polyarylene Polyethers, rejection of claims 1-9, 64, and 68-72 reversed.

Case History and Disposition:

Appeal from Patent and Trademark Office Board of Appeals.

Application for patent of Robert N. Johnson and Alford G. Farnham, Serial No. 230,091, filed Feb. 28, 1972, continuation-in-part of application Serial No. 295,519, filed July 16, 1963. From decision rejecting claims 1-9, 64, and 68-72, applicants appeal. Reversed; Lane, Judge, dissenting in part with opinion.

Attorneys:

Robert C. Brown and Aldo J. Cozzi, both of New York, N.Y. (James C. Arvantes, New York, N.Y., of counsel) for appellants.

Joseph F. Nakamura (Henry W. Tarring, II, of counsel) for Commissioner of Patents and Trademarks.

Judge:

Before Markey, Chief Judge, and Rich, Baldwin, Lane, and Miller, Associate Judges.

Opinion Text

Opinion By:

Markey, Chief Judge.

This appeal is from the decision of the Patent and Trademark Office (PTO) Board of Appeals affirming the rejection under 35 USC 102 or 103 (the rejection also raises a written description issue under 35 USC 112; first paragraph) of claims 1-9, 64, and 68-70 and the rejection under 35 USC 112, first paragraph (enablement) and second paragraph (indefiniteness), of claims 64 and 68-72 in appellants' application No. 230,091 filed February 28, 1972 (the 1972 application) for "Polyarylene Polyethers." ¹ The 1972 application is a continuation-in-part of three earlier applications, the earliest being application No. 295,519 filed July 16, 1963 (the 1963

application). We reverse.

The Invention

The invention is in the field of polymer chemistry and more specifically relates to linear thermoplastic polyarylene polyether polymers composed of recurring units having the general formula

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

where O represents an oxygen atom, ² E represents the residuum of a dihydric phenol ³ compound, and E' represents the residuum of a benzenoid compound having one or more inert electron withdrawing groups ⁴ in the ortho ⁵ or para ⁶ positions to the valence bonds and where both E and E' are bonded to the ether oxygens through aromatic carbon atoms.

Appellants describe a method of synthesizing these polymers by reacting a double alkali metal salt of a dihydric phenol with a dihalobenzenoid compound in the presence of certain solvents under substantially anhydrous reaction conditions.

The 1972 application includes the following disclosure with respect to the electron withdrawing group found in E' and in the E' precursor compound, that is, in the compound which is the predecessor of E' in the above general formula (we have designated paragraphs [A] and [B] and have added emphasis thereto):

Any electron withdrawing group can be employed as the activator group in these compounds. It should be, of course, inert to the reaction, but otherwise its structure is not critical. Preferred are the strong activating groups such as the sulfone group

Page 189

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323. bonding two halogen substituted benzenoid nuclei as in the 4,4'-dichlorodiphenyl sulfone and 4,4'-difluorodiphenyl sulfone, although such other strong withdrawing groups hereinafter mentioned can also be used with equal ease.

The more powerful of the electron withdrawing groups give the fastest reactions and hence are preferred. It is further preferred that the ring contain no electron supplying groups on the same benzenoid nucleus as the halogen; however, the presence of other groups on the nucleus or in the residuum of the compound can be tolerated. Preferably, all of the substituents on the benzenoid nucleus are either hydrogen (zero electron withdrawing), or other groups having a positive sigma a1 value, as set forth in J.F. Bunnett in Chem. Rev. 49 273 (1951) and Quart. Rev., 12, 1 (1958). See also Taft, Steric Effects in Organic Chemistry, John Wiley & Sons (1956), chapter 13; Chem. Rev., 53, 222; JACS, 74, 3120; and JACS, 75, 4231. ⁷

The electron withdrawing group of the dihalobenzenoid compound can function either through the resonance of the aromatic ring, as indicated by those groups having a high sigma a2value, i.e., above about +0.7 or by induction as in perfluoro compounds and like electron sinks.

[A]

Preferably the activating group should have a high sigma a3value, preferably above 1.0, although sufficient activity to promote the reaction is evidenced in those groups having a sigma value above 0.7, although the reaction rate with such a low powered electron withdrawing group may be somewhat low.

The activating group can be basically either of two types:

(a) monovalent groups that activate one or more halogens on the same ring as a nitro group, phenylsulfone, or alkylsulfone, cyano, trifluoromethyl, nitroso, and hetero nitrogen as in pyridine.

(b) divalent group [sic] which can activate displacement of halogens on two different rings, such as the sulfone group

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

; the carbonyl group

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

; the vinyl group

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

; the sulfoxide group

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

; the azo group -N=N-; the saturated fluorocarbon groups -CF₂CF₂-; organic phosphine oxides

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

; where R is a hydrocarbon group, and the ethylidene group

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

where X can be hydrogen or halogen or which can activate halogens on the same ring such as with difluorobenzoquinone, 1,4- or 1,5- or 1,8- difluoroanthraquinone.

[B]

Those skilled in the art will understand that a plurality of electron withdrawing groups may be employed if desired, including electron withdrawing groups having a sigma a4value below about +0.7 provided the cumulative sigma a5influence on each of the reactive halogen groups of the halobenzenoid compound is at least about +0.7.

The Disclosure and Prosecution History of the 1963 Application

To understand the written description issue in this appeal, it is necessary to summarize the disclosure and prosecution history of the 1963 application. The 1963 application described (and claimed) in haec verba a genus of polymers as defined by the above general formula. That application stated:

The high molecular weight polyarylene polyethers of the present invention are the linear thermoplastic reaction products of an alkali metal double salt of a dihydric phenol and a dihalobenzenoid compound. Characteristically, this polymer has a basic structure composed of recurring units having the formula

-O-E-O-E'-

wherein E is the residuum of the dihydric phenol and E' is the residuum of the benzenoid compound, both of which are valently bonded to the ether oxygen through aromatic carbon atoms, as hereinafter more fully discussed. Polymers of this type exhibit excellent strength and toughness properties as well as outstanding thermal, oxidative and chemical stability.

The 1963 application then discussed the identity of E and the E precursor compound, that is, the compound which is the predecessor of E in the general formula. It stated:

The residuum E of the dihydric phenol of these alkali metal salts is not narrowly critical. It can be, for instance, a mononuclear phenylene group as results from hydroquinone and resorcinol, or it may be a di- or polynuclear residuum. Likewise it is possible that the residuum be substituted with other inert nuclear substituents such as halogen, alkyl, alkoxy and like inert substituents.

Such dinuclear phenols can be characterized as having the structure:

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

wherein Ar is an aromatic group and preferably is a phenylene group, Y and Y₁ can be the same or different inert substituent groups as alkyl groups having from 1 to 4 carbon atoms, halogen atoms, i.e. fluorine, chlorine, bromine or iodine, or alkoxy radicals having from 1 to 4 carbon atoms, r and z are integers having a value from 0 to 4, inclusive, and R is representative of a bond between aromatic carbon atoms as in dihydroxydiphenyl, or is a divalent radical, including for example, inorganic radicals as

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

, -O-, -S-, -S-S-, -SO₂-, and divalent organic hydrocarbon radicals such as alkylene, alkylidene, cycloaliphatic, or the halogen, alkyl, aryl or like substituted alkylene, alkylidene and cycloaliphatic radicals as well as alkalicyclic, alkarylene and aromatic radicals and a ring fused to both Ar group[s].

The application then mentioned by name some fifty specific dihydric dinuclear phenol (bisphenol) compounds which could be the E precursor compound. The application further stated:

A preferred form of the polyarylene polyethers of this invention are those prepared using the dihydric polynuclear phenols of the following four types, including the derivatives thereof which are substituted with inert substituent groups

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

in which the R group represents hydrogen, lower alkyl, lower aryl and the halogen substituted groups thereof, which can be the same or different.

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Turning to the identity of the E' precursor compound, the application stated:

Any dihalobenzenoid compound or mixture of dihalobenzenoid compounds

Page 191

can be employed in this invention which compound or compounds has the two halogens bonded to benzene rings having an electron withdrawing group in at least one of the positions ortho and para to the halogen group. The dihalobenzenoid compound can be either mononuclear where the halogens are attached to the same benzenoid ring or polynuclear where they are attached to different benzenoid rings, as long as there is the activating electron withdrawing group in the ortho or para position of that benzenoid nucleus.

The 1963 application also included a discussion of the electron withdrawing group that was substantially the same as the paragraphs quoted above from the 1972 application.

The 1963 application contained twenty-six "examples" disclosing in detail the physical and chemical characteristics of fifteen species of polyarylene polyethers. One of the species was the polymer composed of these recurring structural units (which we designate as species [1]): ⁸
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Another species disclosed was the polymer composed of these recurring structural units (which we designate as species [2]): ⁹
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Appellants' 1963 application became involved in a three-party interference ¹⁰ which resulted in an award of priority adverse to appellants from which they did not appeal. ¹¹ "] The sole count of the interference recited species [1].

After their involvement in the interference ended, appellants filed the 1972 application, and they sought broad claims which would at the same time exclude the subject matter of the lost count.

The Claims

Claim 1, now on appeal, is illustrative of the group of claims (claims 1-9, 64, and 68-70) which seek to exclude the subject matter of the lost count and which are involved in the 35 USC 102 or 103 rejection:

1. A substantially linear thermoplastic polyarylene polyether composed of recurring units having the general formula:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

where E is the residuum of a dihydric phenol and E' is the residuum of a benzenoid compound having an inert electron withdrawing group in one or more of the positions ortho and para to the valence bonds having a sigma a1 value above about +0.7, and where both of said residuum [sic, residua] are valently bonded to the ether oxygens through aromatic carbon atoms *with the provisos that E and E' may not both include a divalent sulfone group and may not both include a divalent carbonyl group linking two aromatic nuclei.* [Emphasis added.]

The first "proviso" in claim 1, that "E and E' may not both include a divalent sulfone group," excludes species [1], the species of the lost count. The second "proviso," that "E and E' * * * may not both include a divalent carbonyl group," excludes species [2], which appellants state is

"analogous" or "equivalent" to species [1].¹²

Claims 64 and 71 are illustrative of the group of claims (claims 64 and 68-72) rejected under 35 USC 112, first and second paragraphs:

64. A substantially linear thermoplastic polyarylene polyether composed of recurring units having the general formula:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

where E is the residuum of a dihydric phenol and E' is the residuum of a

Page 192

benzenoid compound having one or more inert electron withdrawing groups in at least one of the position [sic, positions] ortho and para to the valence bonds having a sigma alvalue *sufficient to activate a halogen atom* and where both of said residuum [sic, residua] are valently bonded to the ether oxygens through aromatic carbon atoms with the provisos that E and E' may not both include a divalent carbonyl group linking two aromatic nuclei. [Emphasis added.]

71. The process for preparing substantially linear polyarylene polyethers which comprises reacting substantially equimolar amounts of an alkali metal double salt of a dihydric phenol with a dihalobenzenoid compound *having halogen atoms activated by an inert electron withdrawing group* in at least one of the positions ortho and para to the halogen atom, under substantially anhydrous conditions and in the liquid phase of an organic solvent having the formula:

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

in which R represents a member of the group consisting of monovalent lower hydrocarbon groups free of aliphatic unsaturation on the alpha carbon atom and, when connected together represents a divalent alkylene group, and Z is an integer from 1 to 2 inclusive. [Emphasis added.]

The Rejections

The sole reference relied upon by the examiner and the board is:

Netherlands 6,408,130 January 18, 1965

Claims 1-9, 64, and 68-70 were rejected under 35 USC 102 or 103 as unpatentable in view of the Netherlands patent, which is a foreign-filed counterpart of appellants' 1963 application.

Before the PTO, appellants conceded that the invention was fully disclosed in the

Netherlands patent. However, appellants contended that the claims are entitled to the benefit of the 1963 filing date under 35 USC 120, ¹³ and therefore the Netherlands patent is not available as a prior art reference.

The examiner and the board were of the view that the claims are not entitled to the 1963 filing date because the presently claimed subject matter is not "described" in the 1963 application as required by the first paragraph of 35 USC 112. ¹⁴ As explained by the board:

The question determinative of the issue at hand is thus whether or not appellants are entitled to the filing date of their parent application Serial No. 295,519, i.e., July 16, 1963. An answer to this question quite obviously depends on what is the invention defined by the instant claims. Is it the same as the one disclosed in [the] parent case or does it differ therefrom in a manner which precludes the instant claims from being afforded the filing date of the parent case?

Under the rationale of the CCPA as set forth in *In re Welstead*, 59 CCPA 1105, 463 F.2d 1110, 174 USPQ 449 (compare also *In re Lukach et al.*, 58 CCPA 1233, 442 F.2d 967, 169 USPQ 795, and *In re Smith [(I)]*, 59 CCPA 1025, 458 F.2d 1389, 173 USPQ 679), which we deem controlling, we are constrained to conclude that the present claims are not entitled to the filing date of appellants' parent case Serial No. 295,519. The claims at issue contain provisos that E and E' may not both include a divalent sulfone group and may not both include a divalent carbonyl group linking two aromatic nuclei. The artificial subgenus thus created in the claims is not described in the parent case and would be new matter if introduced into the parent case. It is thus equally "new matter," i.e., matter new to the present application for

Page 193

which no antecedent basis exists in the parent case. Consequently, appellants are not entitled to rely on the filing date of their parent case to support a new subgenus for which no basis exists in the parent case. The reason why appellants now limit their claims to exclude those species eliminated by the provisos, i.e., loss in an interference, is manifestly immaterial.

Having reached the conclusion that appellants are not entitled to the filing date of their parent case for the subject matter defined by the present claims which delineate a new subgenus not described in the parent case, it follows that the Netherlands patent is a valid reference which, by appellants' own admission, fully meets the claims. The indicated rejection of claims 1-9, 64 and 68-70 under 35 U.S.C. 102 as unpatentable over the Netherlands patent is thus affirmed. The alternative reliance by the Examiner on Section 103 is inconsequential, Section 102 of the statute being the epitome of Section 103. *In re Pearson*, (CCPA), 494 F.2d 1399, 181 USPQ 641.

Claims 64 and 68-72 were rejected under 35 USC 112, first and second paragraphs. In his Answer, the examiner stated that the claims were rejected under §112, first paragraph, for "being

broader than the enabling disclosure" and under §112, second paragraph, ¹⁵ for being "broader than the express limitations disclosed as defining the invention." The examiner said the "specific deficiencies of the claims and disclosure" are that the expression "to activate a halogen" (claim 64) is "indefinite" because "it does not specify toward what the activation is" and that "[t]he express disclosure is clearly limited to the sigma[a1] value recited in claim 1, for example: see [[A] and [B]]."

In affirming the examiner on these rejections, the board stated:

Further, claims 64 and 68-72 stand finally rejected under 35 U.S.C. 112 as being broader than the enabling disclosure (first paragraph) and broader than the express limitations disclosed as defining the invention (paragraph two).

It is the Examiner's position that "to activate a halogen atom" (claim 64) is indefinite and that the disclosure also is limited to dihalobenzenoid compounds not broadly merely "activated by an inert electron withdrawing group" (claims 68-72) but the activation must have a sigma a2value above about +0.7.

We agree with this rejection. The specification makes it quite clear that a minimum sigma a3activation value of the halogen atoms is required (note especially [[A]]) and an undefined sigma a4value thus lacks the requisite preciseness commensurate with the enablement of the disclosure.

Opinion

I. The Rejections of Claims 64 and 68-72 under §112

Claims 64 and 68-72 were rejected under both the first and second paragraphs of 35 USC 112.

[1]We begin with the rejections under the second paragraph of §112. As stated in *In re Moore*, 58 CCPA 1042, 1046-1047, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (1971):

Any analysis in this regard should begin with the determination of whether the claims satisfy the requirements of the second paragraph. * * *

This first inquiry therefore is merely to determine whether the claims do, in fact, set out and circumscribe a particular area with a reasonable degree of precision and particularity. It is here where the definiteness of the language employed must be analyzed -- not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. [Footnote omitted.]

The examiner's §112, second paragraph, rejection was premised on the general ground that the claims are "broader than the express limitations disclosed as defining the invention" and on two specific grounds: (a) that the expression "to activate a halogen atom" is "indefinite" because

"it does not specify toward what the activation is;" and (b) that "[t]he express disclosure is clearly limited to the sigma[a5] value recited in claim 1, for example: see [[A] and [B]]." The board affirmed and stated: "an undefined sigma a6value thus lacks the requisite *preciseness* * * *." (Emphasis added.)

Page 194

Ground (a) focuses on the specific phrase "to activate a halogen atom." But the language is found only in claim 64, not in claims 68-72. Claim 68 recites "a dihalobenzenoid compound having halogen atoms activated by an inert electron withdrawing group," and claims 71 and 72 have a similar recitation. (Claims 69 and 70 depend from claim 68.) Those recitations clearly specify "toward what the activation is," as the examiner would require. Ground (a), therefore, lacks merit with respect to claims 68-72.

[2]Product claim 64 ¹⁶ defines the complete polymer structure by describing the constituents partially in terms of their functions in the reaction and by their linkage into the end-product polymer. The specification provides further guidance on the meaning of the E' term:

It is seen also that as used herein, the E' term defined as being the "residuum of the benzenoid compound" refers to the aromatic or benzenoid residue of the compound *after the removal of the halogen atoms on the benzenoid nucleus*. [Emphasis added.]

It is also clear from the specification as a whole, that two keys to the polymerization reaction are inert electron withdrawing groups particularly positioned on the benzenoid nucleus and a cumulative sigma a1value attributable to those withdrawing groups which is sufficient to activate a halogen atom on that nucleus. If the sigma a2value is not sufficient to activate a halogen atom on the benzenoid nucleus, the reaction will not take place and the polymer will not be made. See *In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (CCPA 1976). The specification adequately details which sigma a3values are sufficient to carry out the reaction, and any person skilled in the art would immediately recognize from the above-quoted portion of the disclosure or the specification as a whole that the halogen atom mentioned in claim 64 was on the benzenoid nucleus prior to the reaction. It is clear that those skilled in the art would have no trouble ascertaining whether any particular polymer falls within the scope of claim 64. See *In re Goffe*, 526 F.2d 1393, 188 USPQ 131 (CCPA 1975). The questioned limitation is merely surplusage, since the claim would be definite with or without it. ¹⁷

[3]The point made by the board, that "an undefined sigma a4value" lacks "preciseness," is also unsound. ¹⁸ Claim language must be read in light of the specification as it would be interpreted by one of ordinary skill in the art. *In re Moore*, supra. As pointed out above, those skilled in the art will be able to determine immediately from appellants' detailed specification what level of activation (i.e., sigma a5value) is necessary to practice the invention. Cf. *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). We conclude that the subject matter embraced by claims 64 and 68-72 is definite and that the claims set out and circumscribe a

particular area with a reasonable degree of precision and particularity. In re Angstadt, *supra*; In re Skoll, 523 F.2d 1392, 187 USPQ 481 (CCPA 1975); In re Watson, 517 F.2d 465, 186 USPQ 11 (CCPA 1975); In re Moore, *supra*. Therefore, the rejection of claims 64 and 68-72 under the *second* paragraph of 35 USC 112 is reversed.

[4]The examiner's general ground and his ground (b) raise a lack of enablement issue properly arising under the *first*, not the *second*, paragraph of §112. Ground (b) simply supplies the examiner's reasoning in support of the rejection of the claims under §112, first paragraph, as "broader than the enabling disclosure."

As appellants state, the crux of this lack of enablement rejection is that although the specification describes how the halogen atoms bonded to the dihalobenzenoid compound (the E' precursor compound) must be activated in order for polymerization to occur, the claims at issue do not recite a numerical definition of the degree of activation (a minimum sigma a6value) required from the electron withdrawing group. The PTO position is that the claims must recite a minimum sigma a7value in order to conform the scope of the claims to the scope of enablement provided by the specification. The PTO relies on statements [A] and [B] to prove that the scope of enablement

Page 195

provided by the specification is not commensurate with the scope of the claims.

[5]First, we note that it is the function of the specification, not the claims, to set forth the "practical limits of operation" of an invention. In re Rainer, 49 CCPA 1243, 1248, 305 F.2d 505, 509, 134 USPQ 343, 346 (1962). One does not look to claims to find out how to practice the invention they define, but to the specification. In re Roberts, 470 F.2d 1399, 1403, 176 USPQ 313, 315 (CCPA 1973); In re Fuetterer, 50 CCPA 1453, 319 F.2d 259, 138 USPQ 217 (1963).

[6]Second, we note that the specification *as a whole* must be considered in determining whether the scope of enablement provided by the specification is commensurate with the scope of the claims. In re Moore, *supra* at 1047, 439 F.2d at 1235, 169 USPQ at 238-39.

The present specification includes broad statements such as: "Any electron withdrawing group can be employed as the activator group in these compounds." The specification also discusses preferred embodiments, alternative embodiments, and the practical limits of operation.

Statement [A] describes preferred embodiments and practical limits of operation. It says that electron withdrawing groups having a high sigma a1value ("preferably above 1.0") are preferred and that the practical limit of operation of the polymerization reaction is reached when the electron withdrawing group has a sigma a2value of 0.7 (at that value the reaction rate "may be somewhat low").

Statement [B] describes an alternative embodiment ("a plurality of electron withdrawing groups") and the practical limit of operation for this embodiment. It states that the cumulative

sigma a3influence should be "at least about +0.7."

[7]The PTO would limit appellants to claims reciting a sigma a4value of at least 0.7. This view is improper because it requires the claims to set forth the practical limits of operation for the invention and it effectively ignores the scope of enablement provided by the specification as a whole. As we said in *In re Goffe*, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976):

[T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts. See *In re Fuetterer*, 50 CCPA 1453, 1462, 319 F.2d 259, 265, 138 USPQ 217, 223 (1963). [Footnote omitted.]

The rejection of claims 64 and 68-72 under the *first* paragraph of 35 USC 112 is reversed.

II. The Rejection of Claims 1-9, 64, and 68-70 Under §102 or §103, Raising Issues Under §112 and §120

[8]We are convinced that the invention recited in claim 1 is "disclosed in the manner provided by the first paragraph of section 112" in the 1963 application and that claim 1 is therefore entitled to the benefit of the 1963 filing date. ¹⁹ The only inquiry is whether, after exclusion from the original claims of two species specifically disclosed in the 1963 application, the 1963 disclosure satisfies §112, first paragraph, for the "limited genus" ²⁰ now claimed.

While the board found that "no antecedent basis exists in the parent case" for the "limited genus" in claim 1, we see more than ample basis for claims of such scope. The 1963 disclosure is clearly directed to polymers of the type claimed. Fifty specific choices are mentioned for the E precursor compound, a broad *class* is identified as embracing suitable *choices* for the E' precursor compound, and twenty-six "examples" are disclosed which detail fifteen species of polyarylene polyethers. Only fourteen of those species and twenty-three of the "examples" are within the scope of the claims now on appeal. Two of the many choices for E and E' precursor compounds are deleted from the protection sought, because appellant is *claiming less* than the full scope of his disclosure. But, as we said in *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976):

Inventions are constantly made which turn out not to be patentable, and applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable.

Page 196

[9]It is for the inventor to decide what *bounds* of protection he will seek. *In re Saunders*, 58

CCPA 1316, 1327, 444 F.2d 599, 607, 170 USPQ 213, 220 (1971). To deny appellants the benefit of their grandparent application in this case would, as this court said in Saunders:

* * * let form triumph over substance, substantially eliminating the right of an applicant to retreat to an otherwise patentable species merely because he erroneously thought he was first with the genus when he filed.

The board cited as "controlling" the decisions of this court in *In re Welstead*, 59 CCPA 1105, 463 F.2d 1110, 174 USPQ 449 (1972); *In re Lukach*, 58 CCPA 1233, 442 F.2d 967, 169 USPQ 795 (1971); and *In re Smith*, 59 CCPA 1025, 458 F.2d 1389, 173 USPQ 679 (1972). Those decisions, because of important factual distinctions, are not controlling.

In *Welstead* the applicant was attempting to introduce into his claims a new subgenus where " * * * the specification * * * contained neither a description * * * of the [subgenus] * * * nor descriptions of the species thereof amounting in the aggregate to the same thing * * *." *Welstead* conceded the absence from his disclosure of compounds of the "second type" within the new subgenus. *Welstead* is thus clearly distinguishable from the present case, in which appellants' grandparent application contains a broad and complete generic disclosure, coupled with extensive examples fully supportive of the limited genus now claimed. Indeed, *Welstead* might have well been cited by the board in support of a decision contrary to that reached, in view of what this court there implied concerning the possibility that "descriptions of species amounting in the aggregate to the same thing" may satisfy the description requirements of 35 USC 112, paragraph one.

Similarly, in *Lukach* we noted that " * * * the grandparent application here does not disclose any defined genus of which the presently claimed copolymers are a subgenus." That is not the fact here. Appellants' grandparent application clearly describes the genus and the two special classes of polymer materials excluded therefrom.

In *Smith* the applicant sought the benefit of his prior application for a broadened generic claim, replacing the claim limitation "at least 12 carbon atoms * * *" with a new limitation calling specifically for 8 to 36 carbon atoms, where there was no disclosure of either the range itself or of a sufficient number of species to establish entitlement to the claimed range. Appellants, in contrast to the applicant in *Smith*, are narrowing their claims, and the full scope of the limited genus now claimed is supported in appellants' earlier application, generically and by specific examples.

[10]The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. All that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count.

[11]The board indicated that "it is manifestly immaterial" *why* appellants limited their claims.

Though it is true that insufficiency under §112 could not be cured by citing the causes for such insufficiency, it is not true that the factual context out of which the question under §112 arises is immaterial. Quite the contrary. Here, as we hold on the facts of this case, the "written description" in the 1963 specification supported the claims in the absence of the limitation, and that specification, having described the whole, necessarily described the part remaining. The facts of the prosecution are properly presented and relied on, under these circumstances, to indicate that appellants are merely excising the invention of another, to which they are not entitled, and are not creating an "artificial subgenus" or claiming "new matter."

In summary, and for the reasons discussed, the rejections of claims 64 and 68-72 under §112, first and second paragraphs, are reversed; appellants' 1963 disclosure satisfied §112, first paragraph, with respect to claims 1-9, 64, and 68-70 and appellants are, therefore, entitled to the benefit of their 1963 filing date under 35 USC 120. The Netherlands patent is thus rendered unavailable as a prior art reference, and the rejection of the claims under 35 USC 102 or 103 is reversed.

Footnotes

Footnote 1. Claims 10-54 and 65-67 stand allowed. A petition for reconsideration was denied by the board.

Footnote 2. The - O - linkages in the general formula are called ether linkages.

Footnote 3. A dihydric phenol is a type of aromatic organic compound in which two hydroxy (-OH) groups are attached directly to a benzene ring.

Footnote 4. An electron withdrawing group is a substituent which withdraws electrons from the aromatic ring to which it is attached.

Footnote 5. An aromatic ring bearing substituents on adjacent carbon atoms is called ortho substituted.

Footnote 6. An aromatic ring bearing substituents on opposite carbon atoms is called para substituted.

Footnote 7. Appellants' brief specifically refers to one of the publications cited (Chem. Rev., 53, 222 [1953]) and states that its author (Jaffe) defines the sigma a1 value as a "special substituent constant" for the "Hammett equation" which is an empirically derived formula intended to show a general quantitative relation between the nature of a given substituent and the reactivity of a side chain. Thus, sigma a2 values are based on experimental data and they measure the "activation energy" of a given substituent (electron withdrawing group).

Footnote 8. The -SO₂- linking group in species [1] is called a sulfone group.

Footnote 9. The -CO- linking group in species [2] is called a carbonyl group.

Footnote 10. Interference No. 95,807, declared February 17, 1967.

Footnote 11. Another party did appeal. See *Vogel v. Jones*, 486 F.2d 1068, 179 USPQ 425 (CCPA 1973).

Footnote 12. The provisos actually exclude more than species [1] and [2]. For example, polymers similar to species [1] and [2] but having substituted ring structures are also excluded.

Footnote 13. §120. Benefit of earlier filing date in the United States.

An application for patent *for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States* by the same inventor shall have the same effect, *as to such invention*, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application. [Emphasis added.]

Footnote 14.

§112. Specification.

The specification shall contain *a written description of the invention*, and of the manner and process of making and using it, *in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same*, and shall set forth the best mode contemplated by the inventor of carrying out his invention. [Emphasis added.]

Footnote 15.

§112. Specification.

* * *

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Footnote 16.

Claims 68-70 are product-by-process claims.

Footnote 17. We do not speculate on whether or not the claim would be unduly broad if the questioned limitation were removed. But undue breadth is not indefiniteness. In *re Borkowski*, 57 CCPA 946, 422 F.2d 904, 164 USPQ 642 (1970). This claim is definite either with or without the phrase "to activate a halogen atom."

Footnote 18. In re Merat, 519 F.2d 1390, 186 USPQ 471 (CCPA 1975), cited by the Solicitor, affirmed a §112, second paragraph, rejection because the same word ("normal") was used in the claims in one sense and in the specification in a different sense, thus rendering the claims indefinite. There is nothing akin to the Merat situation here.

Footnote 19. Appellants have not argued the claims separately, thus, claims 2-9, 64, and 68-70 stand or fall with claim 1.

Footnote 20. Appellants refer to the subject matter recited in claim 1 as a "limited genus." The board called it an "artificial subgenus." We use appellants' terminology. Whatever the label, the issue is the same.

Dissenting Opinion Text

Dissent By:

Lane, Judge, dissenting in part,

I would affirm the rejection of claims 64 and 68-72 under §112, paragraphs 1 and 2, because the specification indicates that a

Page 197

minimum sigma value of +0.7 is an *essential requisite*. These claims fail to recite this requisite, thus fail to define appellants' invention and are broader than the disclosure. I concur in reversing the rejection of claims 1-9.

- End of Case -

In re O'Farrell (CA FC) 7 USPQ2d 1673

In re O'Farrell

**U.S. Court of Appeals Federal Circuit
7 USPQ2d 1673**

**Decided August 10, 1988
No. 87-1486**

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- Evidence of (§ 115.0906)

Applicants' method of producing predetermined protein in stable form in host species of bacteria through genetic engineering is obvious within meaning of 35 USC 103 since reference, authored by two of three patent applicants and published more than one year prior to patent application date, contained detailed enabling methodology for practicing claimed invention, suggestion for modifying prior art to practice claimed invention, and evidence suggesting that invention could be successful, and reference thus rendered invention obvious to those of ordinary skill in art at time invention was made.

2. Patentability/Validity -- Obviousness -- Evidence of (§ 115.0906)

Experimenters' use of heterologous gene coded for ribosomal RNA, which is not ordinarily translated, rather than gene coded for predetermined protein, in plasmid cloning vector for introduction into host bacteria in genetic engineering experiment, does not require finding that applicant's claimed method of producing predetermined protein in host bacteria through genetic

engineering was not obvious in view of published paper describing experiment, particularly observation that hybrid messenger RNA produced by experiment was apparently translated into protein, since it would have been obvious and reasonable to conclude from such observation that if gene coded for ribosomal RNA produced "junk" or "nonsense" protein, then use of gene coded for predetermined protein would result in production of "useful" protein, as application claims.

3. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Rejection of patent application cannot be overturned on ground that examiner and Board of Patent Appeals and Interferences applied impermissible "obvious to try" standard, since assignment of error for application of such standard usually occurs when invention is made by varying all parameters or trying each of numerous choices until successful without indication in prior art as to which parameters were critical or which choices were likely to be successful, or when invention is made by exploring promising new technology or general approach with only general guidance from prior art as to particular form of claimed invention or how to achieve it, and since neither situation is present in instant case.

4. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Finding of obviousness under 35 USC 103 requires only that prior art reveal reasonable expectation of success in producing claimed invention, rather than absolute prediction of such success.

Case History and Disposition:

Page 1673

Appeal from decision of Patent and Trademark Office, Board of Patent Appeals and Interferences.

Patent application, serial no. 180,424, filed by Patrick H. O'Farrell, Barry O. Polisky, and David H. Gelfand. From decision of Board of Patent Appeals and Interferences affirming final rejection of application on grounds of obviousness, applicants appeal. Affirmed.

Attorneys:

J. Bruce McCubbrey of Fitch, Even, Tabin & Flannery (Virginia H. Meyer, with them on brief), San Francisco, Calif., for appellant.

Harris A. Pitlick, associate solicitor, Patent and Trademark Office (Joseph F. Nakamura, solicitor and Fred E. McKelvey, deputy solicitor, with him on brief), for appellee.

Judge:

Before Markey, chief judge, and Rich and Nies, circuit judges.

Opinion Text

Opinion By:

Rich, J.

This appeal is from the decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences (board) affirming the patent examiner's final rejection of patent application Serial No. 180,424, entitled "Method and Hybrid Vector for Regulating Translation of heterologous DNA in Bacteria." The application was rejected under 35 USC 103 on the ground that the claimed invention would have been obvious at the time the invention was made in view of a published paper by two of the three coinventors, and a publication by Bahl, Marians & Wu 1 *Gene* 81 (1976) (Bahl). We affirm.

The claimed invention is from the developing new field of genetic engineering. A broad claim on appeal reads:

Page 1674

Claim 1. A method for producing a predetermined protein in a stable form in a transformed host species of bacteria comprising, providing a cloning vector which includes at least a substantial portion of a gene which is indigenous to the host species of bacteria and is functionally transcribed and translated in that species, said substantial portion of said indigenous gene further including the regulatory DNA sequences for RNA synthesis and protein synthesis but lacking the normal gene termination signal, and linking a natural or synthetic heterologous gene encoding said predetermined protein to said indigenous gene portion at its distal end, said heterologous gene being in proper orientation and having codons arranged in the same reading frame as the codons of said indigenous gene so that readthrough can occur from said indigenous gene portion into said heterologous gene in the same reading frame, said heterologous gene portion further containing sufficient DNA sequences to result in expression of a fused protein having sufficient size so as to confer stability on said predetermined protein when said vector is used to transform said host species of bacteria.

Illustrative embodiments are defined in more specific claims. For example:

Claim 2. A method for producing a predetermined protein in a stable form in a transformed host species of bacteria, comprising, providing an *E. coli* plasmid having an operator, a promoter, a site for the initiation of translation, and at least a substantial portion of the beta-galactosidase gene of the *E. coli* lactose operon, said substantial portion of said beta-galactosidase gene being under the control of said operator, promoter and site for initiation of translation, said substantial portion of said beta-galactosidase gene lacking the normal gene termination signal, and linking a heterologous gene encoding said predetermined protein to said beta-galactosidase gene portion at its distal end, said heterologous gene being in proper orientation and having codons arranged in the same reading frame as the codons of the said beta-galactosidase gene portion so that readthrough can occur from said beta-galactosidase gene portion into said heterologous gene in the same reading frame, said heterologous gene portion further containing sufficient DNA sequences to result in expression of a fused protein having sufficient size so as to confer stability on said predetermined protein when said vector is used to transform said host species of bacteria.

Claim 3. The method of Claim 2 wherein said *E. coli* plasmid comprises the plasmid designated pBGP120.

Although the terms in these claims would be familiar to those of ordinary skill in genetic engineering, they employ a bewildering vocabulary new to those who are not versed in molecular biology. An understanding of the science and technology on which these claims are based is essential before one can analyze and explain whether the claimed invention would have been obvious in light of the prior art.

I. Background 1

Proteins are biological molecules of enormous importance. Proteins include enzymes that catalyze biochemical reactions, major structural materials of the animal body, and many hormones. Numerous patents and applications for patents in the field of biotechnology involve specific proteins or methods for making and using proteins. Many valuable proteins occur in nature only in minute quantities, or are difficult to purify from natural sources. Therefore, a goal of many biotechnology projects, including appellants' claimed invention, is to devise methods to synthesize useful quantities of specific proteins by controlling the mechanism by which living cells make proteins.

The basic organization of all proteins is the same. Proteins are large polymeric molecules consisting of chains of smaller building blocks, called *amino acids*, that are linked together covalently. 2 The chemical bonds linking amino acids together are called *peptide* bonds, so proteins are also called *poly*

Page 1675

peptides. 3 It is the exact sequence in which the amino acids are strung together in a polypeptide chain that determines the identity of a protein and its chemical characteristics. 4 Although there are only 20 amino acids, they are strung together in different orders to produce the hundreds of thousands of proteins found in nature.

To make a protein molecule, a cell needs information about the sequence in which the amino acids must be assembled. The cell uses a long polymeric molecule, DNA (deoxyribonucleic acid), to store this information. The subunits of the DNA chain are called *nucleotides*. A nucleotide consists of a nitrogen-containing ring compound (called a *base*) linked to a 5-carbon sugar that has a phosphate group attached. DNA is composed of only four nucleotides. They differ from each other in the base region of the molecule. The four bases of these subunits are adenine, guanine, cytosine, and thymine (abbreviated respectively as A, G, C and T). The sequence of these bases along the DNA molecule specifies which amino acids will be inserted in sequence into the polypeptide chain of a protein.

DNA molecules do not participate directly in the synthesis of proteins. DNA acts as a permanent "blueprint" of all of the genetic information in the cell, and exists mainly in extremely long strands (called *chromosomes*) containing information coding for the sequences of many proteins, most of which are not being synthesized at any particular moment. The region of DNA on the chromosome that codes for the sequence of a single polypeptide is called a *gene*. In order to *express* a gene (the process whereby the information in a gene is used to synthesize new protein), a copy of the gene is first made as a molecule of RNA (ribonucleic acid).

RNA is a molecule that closely resembles DNA. It differs, however in that it contains a different sugar (ribose instead of deoxyribose) and the base thymine (T) of DNA is replaced in RNA by the structurally similar base, uracil (U). Making an RNA copy of DNA is called *transcription*. The transcribed RNA copy contains sequences of A, U, C, and G that carry the same information as the sequence of A, T, C, and G in the DNA. That RNA molecule, called *messenger RNA*, then moves to a location in the cell where proteins are synthesized.

The code whereby a sequence of nucleotides along an RNA molecule is translated into a sequence of amino acids in a protein (i.e., the "genetic code") is based on serially reading groups of three adjacent nucleotides. Each combination of three adjacent nucleotides, called a *codon*, specifies a particular amino acid. For example, the codon U-G-G in a messenger RNA molecule specifies that there will be a tryptophan molecule in the corresponding location in the corresponding polypeptide. The four bases A, G, C and U can be combined as triplets in 64 different ways, but there are only 20 amino acids to be coded. Thus, most amino acids are coded for by more than one codon. For example, both U-A-U and U-A-C code for tyrosine, and there are six different codons that code for leucine. There are also three codons that do not code for any amino acid (namely, U-A-A, U-G-A, and U-A-G). Like periods at the end of a sentence, these sequences signal the end of the polypeptide chain, and they are therefore called *stop codons*.

The cellular machinery involved in synthesizing proteins is quite complicated, and centers around large structures called *ribosomes* that bind to the messenger RNA. The ribosomes and associated molecules "read" the information in the messenger RNA molecule, literally shifting

along the strand of RNA three nucleotides at a time, adding the amino acid specified by that codon to a growing polypeptide chain that is also attached to the ribosome. When a stop codon is reached, the polypeptide chain is complete and detaches from the ribosome.

The conversion of the information from a sequence of codons in an RNA molecule into the sequence of amino acids in a newly synthesized polypeptide is called *translation*. A messenger RNA molecule is typically reused to make many copies of the same protein. Synthesis of a protein is usually terminated by destroying the messenger RNA. (The information for making more of that protein remains stored in DNA in the chromosomes.)

The translation of messenger RNA begins at a specific sequence of nucleotides that bind the RNA to the ribosome and specify which is the first codon that is to be translated. Translation then proceeds by reading nucleotides, three at a time, until a stop codon is reached. If some error were to occur that shifts the frame in which the nucleotides are read by one or two nucleotides, all of the codons after this shift would be misread. For example, the sequence of codons [. . . C-U-C-A-G-C-G-U-U-A-C-C- A. . .] codes for the chain of amino acids [. . . leucine-serine-valine-threonine-. . .]. If the reading of these groups of three nucleotides is displaced by one nucleotide, such as [. . . C-U-C-A-G-C-G-U-U-A-C-C-A . . .], the resulting peptide chain would consist of [. . . serine-alanine-leucine-proline. . .]. This would be an entirely different peptide, and most probably an undesirable and useless one. Synthesis of a particular protein requires that the correct register or *reading frame* be maintained as the codons in the RNA are translated.

The function of messenger RNA is to carry genetic information (transcribed from DNA) to the protein synthetic machinery of a cell where its information is translated into the amino acid sequence of a protein. However, some kinds of RNA have other roles. For example, ribosomes contain several large strands of RNA that serve a structural function (*ribosomal RNA*).

Chromosomes contain regions of DNA that code for the nucleotide sequences of structural RNAs and these sequences are transcribed to manufacture those RNAs. The DNA sequences coding for structural RNAs are still called genes even though the nucleotide sequence of the structural RNA is never translated into protein.

Man, other animals, plants, protozoa, and yeast are *eucaryotic* (or eukaryotic) organisms: their DNA is packaged in chromosomes in a special compartment of the cell, the nucleus. Bacteria (*procaryotic* or prokaryotic organisms) have a different organization. Their DNA, usually a circular loop, is not contained in any specialized compartment. Despite the incredible differences between them, all organisms, whether eucaryote or procaryote, whether man or mouse or lowly bacterium, use the same molecular rules to make proteins under the control of genes. In all organisms, codons in DNA are transcribed into codons in RNA which is translated on ribosomes into polypeptides according to the same genetic code. Thus, if a gene from a man is transferred into a bacterium, the bacterium can manufacture the human protein. Since most commercially valuable proteins come from man or other eucaryotes while bacteria are essentially little biochemical factories that can be grown in huge quantities, one strategy for manufacturing a desired protein (for example, insulin) is to transfer the gene coding for the protein from the eucaryotic cell where the gene normally occurs into a bacterium.

Bacteria containing genes from a foreign source (*heterologous* genes) integrated into their own genetic makeup are said to be *transformed* . When transformed bacteria grow and divide, the inserted heterologous genes, like all the other genes that are normally present in the bacterium (*indigenous* genes), are replicated and passed on to succeeding generations. One can produce large quantities of transformed bacteria that contain transplanted heterologous genes. The process of making large quantities of identical copies of a gene (or other fragment of DNA) by introducing it into procaryotic cells and then growing those cells is called *cloning* the gene. After growing sufficient quantities of the transformed bacteria, the biotechnologist must induce the transformed bacteria to *express* the cloned gene and make useful quantities of the protein. This is the purpose of the claimed invention.

In order to make a selected protein by expressing its cloned gene in bacteria, several technical hurdles must be overcome. First the gene coding for the specific protein must be isolated for cloning. This is a formidable task, but recombinant DNA technology has armed the genetic engineer with a variety of

Page 1677

techniques to accomplish it. 7 Next the isolated gene must be introduced into the host bacterium. This can be done by incorporating the gene into a cloning vector. A *cloning vector* is a piece of DNA that can be introduced into bacteria and will then replicate itself as the bacterial cells grow and divide. Bacteriophage (viruses that infect bacteria) can be used as cloning vectors, but plasmids were the type used by appellants. A *plasmid* is a small circular loop of DNA found in bacteria, separate from the chromosome, that replicates like a chromosome. It is like a tiny auxilliary chromosome containing only a few genes. Because of their small size, plasmids are convenient for the molecular biologist to isolate and work with. Recombinant DNA technology can be used to modify plasmids by splicing in cloned eucaryotic genes and other useful segments of DNA containing control sequences. Short pieces of DNA can even be designed to have desired nucleotide sequences, synthesized chemically, and spliced into the plasmid. One use of such chemically synthesized linkers is to insure that the inserted gene has the same reading frame as the rest of the plasmid; this is a teaching of the Bahl reference cited against appellants. A plasmid constructed by the molecular geneticist can be inserted into bacteria, where it replicates as the bacteria grow.

Even after a cloned heterologous gene has been successfully inserted into bacteria using a plasmid as a cloning vector, and replicates as the bacteria grow, there is no guarantee that the gene will be expressed, i.e., transcribed and translated into protein. A bacterium such as *E. coli* (the species of bacterium used by appellants) has genes for several thousand proteins. At any given moment many of those genes are not expressed at all. The genetic engineer needs a method to "turn on" the cloned gene and force it to be expressed. This is the problem appellants worked to solve.

II. *Prior art*

Appellants sought to control the expression of cloned heterologous genes inserted into bacteria.

They reported the results of their early efforts in a publication, the three authors of which included two of the three coinventor-appellants (the Polisky reference 8), that is undisputed prior art against them. Their strategy was to link the foreign gene to a highly regulated indigenous gene. Turning on expression of the indigenous gene by normal control mechanisms of the host would cause expression of the linked heterologous gene.

As a controllable indigenous gene, the researchers chose a gene in the bacterium *E. coli* that makes beta-galactosidase. *Beta-galactosidase* is an enzyme needed to digest the sugar, lactose (milk sugar). When *E. coli* grows in a medium that contains no lactose, it does not make beta-galactosidase. If lactose is added to the medium, the gene coding for beta galactosidase is expressed. The bacterial cell makes beta-galactosidase and is then able to use lactose as a food source. When lactose is no longer available, the cell again stops expressing the gene for beta galactosidase.

The molecular mechanisms through which the presence of lactose turns on expression of the beta-galactosidase gene has been studied in detail, and is one of the best understood examples of how gene expression is regulated on the molecular level. The beta-galactosidase gene is controlled by segments of DNA adjacent to the gene. These *regulatory DNA sequences* (the general term used in Claim 1) include the *operator* and *promoter* sequences (specified in Claim 2). 9 The researchers constructed a plasmid containing the beta-galactosidase gene with its operator and promoter. This gene (with its regulatory sequences) was removed from the chromosome of *E. coli* where it is normally found and was transplanted to a plasmid that could be conveniently manipulated.

Restriction endonucleases are useful tools in genetic engineering. These enzymes cut strands of DNA, but only at places where a specific sequence of nucleotides is present. For example, one restriction endonuclease, called *EcoRI* , cuts DNA only at sites where

Page 1678

the nucleotide sequence is [. . .-G-A-A-T-T-C-. . .]. With restriction enzymes the genetic engineer can cut a strand of DNA at very specific sites into just a few pieces. With the help of "repair" enzymes, other pieces of DNA can be spliced onto the cut ends. The investigators found that the plasmid which they had constructed contained only two sequences that were cut by *EcoRI*. They were able to eliminate one of these sites that was unwanted. They were then left with a plasmid containing the beta-galactosidase gene with its regulatory sequences, and a single *EcoRI* site that was within the beta-galactosidase gene and close to its stop codon. They named this plasmid that they had constructed pBGP120.

The next step was to cut the plasmid open at its *EcoRI* site and insert a heterologous gene from another organism. The particular heterologous gene they chose to splice in was a segment of DNA from a frog that coded for ribosomal RNA. The frog gene was chosen as a test gene for reasons of convenience and availability. The new plasmid created by inserting the frog gene was similar to pBGP120, but its beta-galactosidase gene was incomplete. Some codons including the stop codon were missing from its end, which instead continued on with the sequence of the frog

ribosomal RNA gene. The investigators named this new plasmid pBGP123. They inserted this plasmid back into *E. coli* and grew sufficient quantities for study. They then fed the *E. coli* with lactose. As they had intended, the lactose turned on transcription of the beta-galactosidase gene in the plasmid. RNA polymerase moved along the plasmid producing a strange new kind of RNA: Each long strand of RNA first contained codons for the messenger RNA for beta-galactosidase and then continued without interruption with the codons for the frog ribosomal RNA. Thus, there was *read-through* transcription in which the RNA polymerase first transcribed the indigenous (beta-galactosidase) gene and then "read through," i.e., continued into and through the adjacent heterologous (frog ribosomal RNA) gene. Although the RNA produced was a hybrid, it nevertheless contained a nucleotide sequence dictated by DNA from a frog. The researchers had achieved the first controlled transcription of an animal gene inside a bacterium. The researchers had used a gene coding for a ribosomal RNA as their heterologous test gene. Ribosomal RNA is not normally translated into protein. Nevertheless, they were obviously interested in using their approach to make heterologous proteins in bacteria. They therefore examined the beta-galactosidase made by their transformed bacteria. Patrick O'Farrell, who was not a coauthor of the Polisky paper but was to become a coinventor in the patent application, joined as a collaborator. They found that beta-galactosidase from the transformed bacteria had a higher molecular weight than was normal. They concluded that the bacteria must have used their strange new hybrid RNA like any other messenger RNA and translated it into protein. When the machinery of protein synthesis reached the premature end of the sequence coding for beta-galactosidase it continued right on, three nucleotides at a time, adding whatever amino acid was coded for by those nucleotides, until a triplet was reached with the sequence of a stop codon. The resulting polypeptide chains had more amino acids than normal beta-galactosidase, and thus a higher molecular weight. The researchers published their preliminary results in the Polisky article. They wrote:

If the normal translational stop signals for [beta]-galactosidase are missing in pBGP120, in-phase translational readthrough into adjacent inserted sequences might occur, resulting in a significant increase in the size of the [beta]-galactosidase polypeptide subunit. In fact, we have recently observed that induced cultures of pBGP123 contain elevated levels of [beta]-galactosidase of higher subunit molecular weight than wild-type enzyme (P. O'Farrell, unpublished experiments). We believe this increase results from translation of *Xenopus* [frog] RNA sequences covalently linked to [messenger] RNA for [beta]-galactosidase, resulting in a fused polypeptide. Polisky at 3904.

Since ribosomal RNA is never translated in normal cells, the polypeptide chain produced by translating that chain was not a naturally occurring, identified protein. The authors of the Polisky paper explicitly pointed out that if one were to insert a heterologous gene coding for a protein into their plasmid, it should produce a "fused protein" consisting of a polypeptide made of beta-galactosidase plus the protein coded for by the inserted gene, joined by a peptide bond into a single continuous polypeptide chain:

It would be interesting to examine the expression of a normally translated eukaryotic sequence in pBGP120. If an inserted sequence contains a ribosome binding site that can be utilized in

bacteria, production of high levels of a readthrough transcript might allow for extensive translation of a functional eukaryotic polypeptide. In the absence of an independent ribosome bind

Page 1679

ing site, the eukaryotic sequence would be translated to yield a peptide covalently linked to [beta]-galactosidase. The extent of readthrough translation under *lac* control will depend on the number of translatable codons between the EcoRI site and the first in-phase nonsense [i.e., stop] codon in the inserted sequence.

Id.

III. The Claimed Invention

Referring back to Claims 1 through 3, it can be seen that virtually everything in the claims was present in the prior art Polisky article. The main difference is that in Polisky the heterologous gene was a gene for ribosomal RNA while the claimed invention substitutes a gene coding for a predetermined protein. Ribosomal RNA gene is not normally translated into protein, so expression of the heterologous gene was studied mainly in terms of transcription into RNA. Nevertheless, Polisky mentioned preliminary evidence that the transcript of the ribosomal RNA gene was translated into protein. Polisky further predicted that if a gene that codes for a protein were to be substituted for the ribosomal RNA gene, "a readthrough transcript might allow for extensive translation of a functional eukaryotic polypeptide." Thus, the prior art explicitly suggested the substitution that is the difference between the claimed invention and the prior art, and presented preliminary evidence suggesting that the method could be used to make proteins. Appellants reduced their invention to practice some time in 1976 and reported their results in a paper that was published in 1978. 10 During 1977 they communicated their results to another group of researchers who used the readthrough translation approach to achieve the first synthesis of a human protein in bacteria. 11 Appellants filed an application to patent their invention on August 9, 1978, of which the application on appeal is a division.

IV. The Obviousness Rejection

The application was rejected under 35 USC 103. The position of the examiner and the Board is, simply, that so much of the appellant's method was revealed in the Polisky reference that making a protein by substituting its gene for the ribosomal RNA gene in Polisky (as suggested by Polisky) would have been obvious to one of ordinary skill in the art at the time that the invention was made.

The claims specify that the heterologous gene should be inserted into the plasmid in the same orientation and with the same reading frame as the preceding portion of the indigenous gene. In view of this limitation, the §103 rejection was based either on Polisky alone (supplemented by the fact that the importance of orientation and reading frame was well known in the prior art) or in combination with the Bahl reference which describes a general method for inserting a piece of chemically synthesized DNA into a plasmid. Bahl teaches that this technique could be used to

shift the sequence of DNA inserted into a plasmid into the proper reading frame. Appellants argue that at the time the Polisky article was published, there was significant unpredictability in the field of molecular biology so that the Polisky article would not have rendered the claimed method obvious to one of ordinary skill in the art. Even though there was speculation in the article that genes coding for proteins could be substituted for the ribosomal RNA gene and would be expressed as readthrough translation into the protein, this had never been done. Appellants say that it was not yet certain whether a heterologous protein could actually be produced in bacteria, and if it could, whether additional mechanisms or methods would be required. They contend

Page 1680

that without such certainty the predictions in the Polisky paper, which hindsight now shows to have been correct, were merely invitations to those skilled in the art to try to make the claimed invention. They argue that the rejection amounts to the application of a standard of "obvious to try" to the field of molecular biology, a standard which this court and its predecessors have repeatedly rejected as improper grounds for a §103 rejection. *E.g.*, *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988); *In re Geiger*, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); *In re Merck & Co., Inc.*, 800 F.2d 1091, 1097, 231 USPQ 375, 379 (Fed. Cir. 1986); *In re Antonie*, 559 F.2d 618, 620, 195 USPQ 6, 8 (CCPA 1977). Obviousness under §103 is a question of law. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568, 1 USPQ2d 1593, 1597 (Fed. Cir.), *cert. denied*, 107 S.Ct. 2187 (1987). An analysis of obviousness must be based on several factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviousness, if any. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). *See, e.g.*, *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 958, 1 USPQ2d 1196, 1197 (Fed. Cir. 1986). The scope and content of the prior art and the differences between the prior art and the claimed invention have been examined in sections II and III, *supra*. Appellants say that in 1976 those of ordinary skill in the arts of molecular biology and recombinant DNA technology were research scientists who had "extraordinary skill in relevant arts" and "were among the brightest biologists in the world." Objective evidence of nonobviousness was not argued.

[1] With the statutory factors as expounded by *Graham* in mind and considering all of the evidence, this court must determine the correctness of the board's legal determination that the claimed invention as a whole would have been obvious to a person having ordinary skill in the art at the time the invention was made. We agree with the board that appellants' claimed invention would have been obvious in light of the Polisky reference alone or in combination with Bahl within the meaning of §103. Polisky contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful.

[2] Appellants argue that after the publication of Polisky, successful synthesis of protein was still uncertain. They belittle the predictive value of the observation that expression of the transcribed RNA in Polisky produced beta-galactosidase with a greater than normal molecular weight, arguing that since ribosomal RNA is not normally translated, the polypeptide chains that were added to the end of the beta-galactosidase were "junk" or "nonsense" proteins. This characterization ignores the clear implications of the reported observations. The Polisky study directly proved that a readthrough transcript messenger RNA had been produced. The preliminary observation showed that this messenger RNA was read and used for successful translation. It was well known in the art that ribosomal RNA was made of the same nucleotides as messenger RNA, that any sequence of nucleotides could be read in groups of three as codons, and that reading these codons should specify a polypeptide chain that would elongate until a stop codon was encountered. The preliminary observations thus showed that codons beyond the end of the beta-galactosidase gene were being translated into peptide chains. This would reasonably suggest to one skilled in the art that if the codons inserted beyond the end of the beta-galactosidase gene coded for a "predetermined protein," that protein would be produced. In other words, it would have been obvious and reasonable to conclude from the observation reported in Polisky that since nonsense RNA produced nonsense polypeptides, if meaningful RNA was inserted instead of ribosomal RNA, useful protein would be the result. The relative shortness of the added chains is also not a source of uncertainty, since one skilled in the art would have known that a random sequence of nucleotides would produce a stop codon before the chain got too long. 12

Appellants complain that since predetermined proteins had not yet been produced in transformed bacteria, there was uncertainty as to whether this could be done, and that the rejection is thus founded on an impermissible "obvious to try" standard. It is true that this court and its predecessors have repeatedly emphasized that "obvious to try" is not the standard under §103. However, the meaning of this maxim is sometime lost. Any invention that would in fact have been obvious under §103 would also have been, in a sense, obvious to try. The question is: when is an

Page 1681

invention that was obvious to try nevertheless nonobvious?

[3] The admonition that "obvious to try" is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. *E.g.*, *In re Geiger*, 815 F.2d at 688, 2 USPQ2d at 1278; *Novo Industri A/S v. Travenol Laboratories, Inc.*, 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); *In re Yates*, 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); *In re Antonie*, 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach that

seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. *In re Dow Chemical Co.*, 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1986), *cert. denied*, 107 S.Ct. 1606 (1987); *In re Tomlinson*, 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966). Neither of these situations applies here.

[4] Obviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious. *In re Merck & Co.*, 800 F.2d at 1098, 231 USPQ at 380; *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1461, 221 USPQ 481, 488 (Fed. Cir. 1984); *In re Papesch*, 315 F.2d 381, 386-87, 137 USPQ 43, 47-48 (CCPA 1963). For obviousness under §103, all that is required is a reasonable expectation of success. *In re Longi*, 759 F.2d 887, 897, 225 USPQ 645, 651-52 (Fed. Cir. 1985); *In re Clinton*, 527 F.2d 1226, 1228, 188 USPQ 365, 367 (CCPA 1976). The information in the Polisky reference, when combined with the Bahl reference provided such a reasonable expectation of success.

Appellants published their pioneering studies of the expression of frog ribosomal RNA genes in bacteria more than a year before they applied for a patent. After providing virtually all of their method to the public without applying for a patent within a year, they foreclosed themselves from obtaining a patent on a method that would have been obvious from their publication to those of ordinary skill in the art, with or without the disclosures of other prior art. The decision of the board is

AFFIRMED .

Footnotes

Footnote 1. Basic background information about molecular biology and genetic engineering, can be found in Alberts, Bray, Lewis, Raff, Roberts & Watson, *The Molecular Biology of the Cell*, 1-253, 385-481 (1983) [hereinafter *The Cell*]; Watson, Hopkins, Roberts, Steitz & Weiner, *The Molecular Biology of the Gene*, Vol. 1 (4th ed., 1987) 3-502 [hereinafter *The Gene*]. These standard textbooks were used to supplement the information in the glossary supplied by appellants. The description here is necessarily simplified and omits important facts and concepts that are not necessary for the analysis of this case.

Footnote 2. There are twenty amino acids: alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan, glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine, aspartic acid, glutamic acid, lysine, arginine, and histidine.

Footnote 3. Proteins are often loosely called *peptides*, but technically proteins are only the larger peptides with chains of at least 50 amino acids, and more typically hundreds of amino acids. Some proteins consist of several polypeptide chains bound together covalently or noncovalently. The term "peptide" is broader than "protein" and also includes small chains of amino acids linked by peptide bonds, some as small as two amino acids. Certain small peptides have commercial or medical significance.

Footnote 4. Polypeptide chains fold up into complex 3-dimensional shapes. It is the shape that actually determines many chemical properties of the protein. However, the configuration of a protein molecule is determined by its amino acid sequence. *The Cell* at 111-12; *The Gene* at 50-54.

Footnote 5. The sugar in DNA is deoxyribose, while the sugar in RNA, *infra*, is ribose. The sugar and phosphate groups are linked covalently to those of adjacent nucleotides to form the backbone of the long unbranched DNA molecule. The bases project from the chain, and serve as the "alphabet" of the genetic code.

DNA molecules actually consist of two chains tightly entwined as a double helix. The chains are not identical but instead are complementary: each A on one chain is paired with a T on the other chain, and each C has a corresponding G. The chains are held together by noncovalent bonds between these complementary bases. This double helical structure plays an essential role in the replication of DNA and the transmission of genetic information. *See generally The Cell* at 98-106; *The Gene* at 65-79. However, the information of only one strand is used for directing protein synthesis, and it is not necessary to discuss the implication of the double-stranded structure of DNA here. RNA molecules, *infra*, are single stranded.

Footnote 6. Chromosomes also contain regions of DNA that are not part of genes, i.e., do not code for the sequence of amino acids in proteins. These include sections of DNA adjacent to genes that are involved in the control of transcription, *infra*, and regions of unknown function.

Footnote 7. *See The Cell* at 185-194; *The Gene* at 208-10.

Footnote 8. Polisky, Bishop & Gelfand, *A plasmid cloning vehicle allowing regulated expression of eukaryotic DNA in bacteria*, 73 Proc. Nat'l Acad. Sci. USA 3900 (1976).

Footnote 9. The *promoter* is a sequence of nucleotides where the enzyme that synthesizes RNA, *RNA polymerase*, attaches to the DNA to start the transcription of the beta-galactosidase gene. The *operator* is an overlapping DNA sequence that binds a small protein present in the cell, the lactose repressor protein. The lactose repressor protein binds to the operator and physically blocks the RNA polymerase from properly attaching to the promoter so that transcription cannot proceed. Lactose molecules interact with the lactose repressor protein and cause it to change its shape; after this change in shape it moves out of the way and no longer prevents the RNA polymerase from binding to the promoter. Messenger RNA coding for beta-galactosidase can then be transcribed. *See generally The Cell* at 438-39; *The Gene* at 474-80.

Footnote 10. O'Farrell, Polisk & Gelfand, *Regulated expression by readthrough translation from a plasmid-encoded beta-galactosidase*, 134 J. Bacteriol. 645 (1978). The heterologous genes expressed in these studies were not predetermined, but were instead unidentified genes of unknown origin. The authors speculated that they were probably genes from *E. coli* that were

contaminants in the source of beta-galactosidase genes. *Id.* at 648

Footnote 11. Itakura, Hirose, Crea, Riggs, Heynecker, Bolivar & Boyer, *Expression in Escherichia coli of a chemically synthesized gene for the hormone somatostatin*, 198 Science 1056 (1977). A pioneering accomplishment of the Itakura group is that the gene was not from a human source, but instead was entirely synthesized in the laboratory using chemical methods. It is not clear whether the appellants communicated only the results reported in the Polisky publication or whether they communicated the complete claimed invention.

Footnote 12. The patent application indicates that chains as long as 60 amino acids were added, which is hardly a trivial length of polypeptide.

- End of Case -

In re Deuel (CA FC) 34 USPQ2d 1210

In re Deuel

**U.S. Court of Appeals Federal Circuit
34 USPQ2d 1210**

**Decided March 28, 1995
No. 94-1202**

Headnotes

PATENTS

**1. Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions
(§ 115.0903.03)**

Existence of general method of isolating cDNA or DNA molecules is essentially irrelevant to question of whether specific molecules themselves would have been obvious, in absence of other prior art that suggests claimed DNAs, nor does fact that general process can be conceived in advance for preparing undefined compound mean that claimed specific compound was precisely envisioned and therefore obvious; Board of Patent Appeals and Interferences thus erred by rejecting claims for isolated and purified

Page 1211

DNA and cDNA molecules encoding heparin-binding growth factors based upon alleged obviousness of method of making molecules, since applied references do not teach or suggest claimed cDNA molecules.

Case History and Disposition:

Page 1211

Appeal from the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences; 33 USPQ2d 1445 .

Application for patent filed by Thomas F. Deuel, Yue-Sheng Li, Ned R. Siegel, and Peter G. Milner, serial no. 07/542,232). From decision of the Board of Patent Appeals and Interferences affirming examiner's final rejection of claims, applicants appeal. Reversed.

Attorneys:

G. Harley Blosser and Donald G. Leavit, of Senniger, Powers, Leavitt & Roedel, St. Louis, Mo., for appellants.

Donald S. Chisum, of Morrison & Foerster, Seattle, Wash.; Debra A. Shetka, of Morrison & Foerster, Palo Alto, Calif.; and Robert P. Blackburn, Emeryville, Calif., for amicus curiae The Biotechnology Industry Association and The Bay Area Bioscience Center.

Teddy S. Gron, acting associate solicitor, Albin F. Drost, acting solicitor, and Nancy J. Linck, office of the solicitor, Arlington, Va., for appellee.

Judge:

Before Archer, chief judge, Nies and Lourie, circuit judges.

Opinion Text

Opinion By:

Lourie, J.

Thomas F. Deuel, Yue-Sheng Li, Ned R. Siegel, and Peter G. Milner (collectively "Deuel") appeal from the November 30, 1993 decision of the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences affirming the examiner's final rejection of claims 4-7 of

application Serial No. 07/542,232, entitled "Heparin-Binding Growth Factor," as unpatentable on the ground of obviousness under 35 U.S.C. Section 103 (1988). *Ex parte Deuel*, 33 USPQ2d 1445 (Bd. Pat. App. Int. 1993). Because the Board erred in concluding that Deuel's claims 5 and 7 directed to specific cDNA molecules would have been obvious in light of the applied references, and no other basis exists in the record to support the rejection with respect to claims 4 and 6 generically covering all possible DNA molecules coding for the disclosed proteins, we reverse.

BACKGROUND

The claimed invention relates to isolated and purified DNA and cDNA molecules encoding heparin-binding growth factors ("HBGFs"). HBGFs are proteins that stimulate mitogenic activity (cell division) and thus facilitate the repair or replacement of damaged or diseased tissue. DNA (deoxyribonucleic acid) is a generic term which encompasses an enormous number of complex macromolecules made up of nucleotide units. DNAs consist of four different nucleotides containing the nitrogenous bases adenine, guanine, cytosine, and thymine. A sequential grouping of three such nucleotides (a "codon") codes for one amino acid. A DNA's sequence of codons thus determines the sequence of amino acids assembled during protein synthesis. Since there are 64 possible codons, but only 20 natural amino acids, most amino acids are coded for by more than one codon. This is referred to as the "redundancy" or "degeneracy" of the genetic code.

DNA functions as a blueprint of an organism's genetic information. It is the major component of genes, which are located on chromosomes in the cell nucleus. Only a small part of chromosomal DNA encodes functional proteins.

Messenger ribonucleic acid ("mRNA") is a similar molecule that is made or transcribed from DNA as part of the process of protein synthesis. Complementary DNA ("cDNA") is a complementary copy ("clone") of mRNA, made in the laboratory by reverse transcription of mRNA. Like mRNA, cDNA contains only the protein-encoding regions of DNA. Thus, once a cDNA's nucleotide sequence is known, the amino acid sequence of the protein for which it codes may be predicted using the genetic code relationship between codons and amino acids. The reverse is not true, however, due to the degeneracy of the code. Many other DNAs may code for a particular protein. The functional relationships between DNA, mRNA, cDNA, and a protein may conveniently be expressed as follows:



Collections ("libraries") of DNA and cDNA molecules derived from various

species may be constructed in the laboratory or obtained from commercial sources. Complementary DNA libraries contain a mixture of cDNA clones reverse-transcribed from the

mRNAs found in a specific tissue source. Complementary DNA libraries are tissue-specific because proteins and their corresponding mRNAs are only made ("expressed") in specific tissues, depending upon the protein. Genomic DNA ("gDNA") libraries, by contrast, theoretically contain all of a species' chromosomal DNA. The molecules present in cDNA and DNA libraries may be of unknown function and chemical structure, and the proteins which they encode may be unknown. However, one may attempt to retrieve molecules of interest from cDNA or gDNA libraries by screening such libraries with a gene probe, which is a synthetic radiolabelled nucleic acid sequence designed to bond ("hybridize") with a target complementary base sequence. Such "gene cloning" techniques thus exploit the fact that the bases in DNA always hybridize in complementary pairs: adenine bonds with thymine and guanine bonds with cytosine. A gene probe for potentially isolating DNA or cDNA encoding a protein may be designed once the protein's amino acid sequence, or a portion thereof, is known.

As disclosed in Deuel's patent application, Deuel isolated and purified HBGF from bovine uterine tissue, found that it exhibited mitogenic activity, and determined the first 25 amino acids of the protein's N-terminal sequence. Deuel then isolated a cDNA molecule encoding bovine uterine HBGF by screening a bovine uterine cDNA library with an oligonucleotide probe designed using the experimentally determined N-terminal sequence of the HBGF. Deuel purified and sequenced the cDNA molecule, which was found to consist of a sequence of 1196 nucleotide base pairs. From the cDNA's nucleotide sequence, Deuel then predicted the complete amino acid sequence of bovine uterine HBGF disclosed in Deuel's application.

Deuel also isolated a cDNA molecule encoding human placental HBGF by screening a human placental cDNA library using the isolated bovine uterine cDNA clone as a probe. Deuel purified and sequenced the human placental cDNA clone, which was found to consist of a sequence of 961 nucleotide base pairs. From the nucleotide sequence of the cDNA molecule encoding human placental HBGF, Deuel predicted the complete amino acid sequence of human placental HBGF disclosed in Deuel's application. The predicted human placental and bovine uterine HBGFs each have 168 amino acids and calculated molecular weights of 18.9 kD. Of the 168 amino acids present in the two HBGFs discovered by Deuel, 163 are identical. Deuel's application does not describe the chemical structure of, or state how to isolate and purify, any DNA or cDNA molecule except the disclosed human placental and bovine uterine cDNAs, which are the subject of claims 5 and 7.

Claims 4-7 on appeal are all independent claims and read, in relevant part, as follows:

4. A purified and isolated DNA sequence consisting of a sequence encoding human heparin binding growth factor of 168 amino acids having the following amino acid sequence:

Met Gln Ala . . . [remainder of 168 amino acid sequence].

5. The purified and isolated cDNA of human heparin-binding growth factor having the following nucleotide sequence:

GTCAAAGGCA . . . [remainder of 961 nucleotide sequence].

6. A purified and isolated DNA sequence consisting of a sequence encoding bovine heparin binding growth factor of 168 amino acids having the following amino acid sequence:

Met Gln Thr . . . [remainder of 168 amino acid sequence].

7. The purified and isolated cDNA of bovine heparin-binding growth factor having the following nucleotide sequence:

GAGTGGAGAG . . . [remainder of 1196 nucleotide sequence].

Claims 4 and 6 generically encompass *all* isolated/purified DNA sequences (natural and synthetic) encoding human and bovine HBGFs, despite the fact that Deuel's application does not describe the chemical structure of, or tell how to obtain, any DNA or cDNA except the two disclosed cDNA molecules. Because of the redundancy of the genetic code, claims 4 and 6 each encompass an enormous number of DNA molecules, including the isolated/purified chromosomal DNAs encoding the human and bovine proteins. Claims 5 and 7, on the other hand, are directed to the specifically disclosed cDNA molecules encoding human and bovine HBGFs, respectively.

During prosecution, the examiner rejected claims 4-7 under 35 U.S.C. Section 103 as unpatentable over the combined teachings of

Page 1213

Bohlen 3 and Maniatis. 4 The Bohlen reference discloses a group of protein growth factors designated as heparin-binding brain mitogens ("HBBMs") useful in treating burns and promoting the formation, maintenance, and repair of tissue, particularly neural tissue. Bohlen isolated three such HBBMs from human and bovine brain tissue. These proteins have respective molecular weights of 15 kD, 16 kD, and 18 kD. Bohlen determined the first 19 amino acids of the proteins' N-terminal sequences, which were found to be identical for human and bovine HBBMs. 5 Bohlen teaches that HBBMs are brain-specific, and suggests that the proteins may be homologous between species. The reference provides no teachings concerning DNA or cDNA coding for HBBMs.

Maniatis describes a method of isolating DNAs or cDNAs by screening a DNA or cDNA library with a gene probe. The reference outlines a general technique for cloning a gene; it does not describe how to isolate a particular DNA or cDNA molecule. Maniatis does not discuss certain steps necessary to isolate a target cDNA, *e.g.*, selecting a tissue-specific cDNA library containing a target cDNA and designing an oligonucleotide probe that will hybridize with the target cDNA.

The examiner asserted that, given Bohlen's disclosure of a heparin-binding protein and its N-terminal sequence and Maniatis's gene cloning method, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to clone a gene for HBGF. 6 According to the examiner, Bohlen's published N-terminal sequence would have motivated a person of ordinary skill in the art to clone such a gene because cloning the gene would allow recombinant production of HBGF, a useful protein. The examiner reasoned that a person of ordinary skill in the art could have designed a gene probe based on Bohlen's disclosed N-terminal sequence, then screened a DNA library in accordance with Maniatis's gene cloning method to isolate a gene encoding an HBGF. The examiner did not distinguish between claims 4 and 6 generically directed to all DNA sequences encoding human and bovine HBGFs and

claims 5 and 7 reciting particular cDNAs.

In reply, Deuel argued, *inter alia*, that Bohlen teaches away from the claimed cDNA molecules because Bohlen suggests that HBBMs are brain-specific and, thus, a person of ordinary skill in the art would not have tried to isolate corresponding cDNA clones from human placental and bovine uterine cDNA libraries. The examiner made the rejection final, however, asserting that

[t]he starting materials are not relevant in this case, because it was well known in the art at the time the invention was made that proteins, especially the general class of heparin binding proteins, are highly homologous between species and tissue type. It would have been entirely obvious to attempt to isolate a known protein from different tissue types and even different species.

No prior art was cited to support the proposition that it would have been obvious to screen human placental and bovine uterine cDNA libraries for the claimed cDNA clones. Presumably, the examiner was relying on Bohlen's suggestion that HBBMs may be homologous between species, although the examiner did not explain how homology between species suggests homology between tissue types.

The Board affirmed the examiner's final rejection. In its opening remarks, the Board noted that it is "constantly advised by the patent examiners, who are highly skilled in this art, that cloning procedures are routine in the art." According to the Board, "the examiners urge that when the sequence of a protein is placed into the public domain, the gene is also placed into the public domain because of the routine nature of cloning techniques." Addressing the rejection at issue, the Board determined that Bohlen's disclosure of the existence and isolation of HBBM, a functional protein, would also advise a person of ordinary skill in the art that a gene exists encoding HBBM. The Board found that a person of ordinary skill in the art would have been motivated to isolate such a gene because the protein has useful mitogenic properties, and isolating the gene for HBBM would permit large quantities of the protein to be produced for study and possible commercial use. Like the examiner,

Page 1214

the Board asserted, without explanation, that HBBMs are the same as HBGFs and that the genes encoding these proteins are identical. The Board concluded that "the Bohlen reference would have suggested to those of ordinary skill in this art that they should make the gene, and the Maniatis reference would have taught a technique for 'making' the gene with a reasonable expectation of success." Responding to Deuel's argument that the claimed cDNA clones were isolated from human placental and bovine uterine cDNA libraries, whereas the combined teachings of Bohlen and Maniatis would only have suggested screening a brain tissue cDNA library, the Board stated that "the claims before us are directed to the product and not the method of isolation. Appellants have not shown that the claimed DNA was not present in and could not have been readily isolated from the brain tissue utilized by Bohlen." Deuel now appeals. 7

DISCUSSION

Obviousness is a question of law, which we review *de novo*, though factual findings underlying the Board's obviousness determination are reviewed for clear error. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Woodruff*, 919 F.2d 1575, 1577, 16 USPQ2d 1934, 1935 (Fed. Cir. 1990). The examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if this burden is met does the burden of coming forward with rebuttal argument or evidence shift to the applicant. *Rijckaert*, 9 F.3d at 1532, 28 USPQ2d at 1956. When the references cited by the examiner fail to establish a *prima facie* case of obviousness, the rejection is improper and will be overturned. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

On appeal, Deuel challenges the Board's determination that the applied references establish a *prima facie* case of obviousness. In response, the PTO maintains that the claimed invention would have been *prima facie* obvious over the combined teachings of Bohlen and Maniatis. Thus, the appeal raises the important question whether the combination of a prior art reference teaching a method of gene cloning, together with a reference disclosing a partial amino acid sequence of a protein, may render DNA and cDNA molecules encoding the protein *prima facie* obvious under Section 103.

[1] Deuel argues that the PTO failed to follow the proper legal standard in determining that the claimed cDNA molecules would have been *prima facie* obvious despite the lack of structurally similar compounds in the prior art. Deuel argues that the PTO has not cited a reference teaching cDNA molecules, but instead has improperly rejected the claims based on the alleged obviousness of a method of making the molecules. We agree.

Because Deuel claims new chemical entities in structural terms, a *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art. Normally a *prima facie* case of obviousness is based upon structural similarity, *i.e.*, an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties. Similarly, a known compound may suggest its analogs or isomers, either geometric isomers (*cis v. trans*) or position isomers (*e.g.*, *ortho v. para*).

In all of these cases, however, the prior art teaches a specific, structurally-definable compound and the question becomes whether the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention. See *In re Jones*, 958 F.2d 347, 351, 21 USPQ2d 1941, 1944 (Fed. Cir. 1992); *In re Dillon*, 919 F.2d 688, 692, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (*en banc*) ("structural similarity between claimed and prior art subject matter, . . . where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness"), *cert. denied*, 500 U.S. 904 (1991); *In re Grabiak*, 769 F.2d 729, 731-32, 226 USPQ 870, 872 (Fed. Cir. 1985) ("[I]n the

case before us there must be adequate support in the prior art for the [prior art] ester/ [claimed] thioester change in structure, in order to complete the PTO's *prima facie*

Page 1215

case and shift the burden of going forward to the applicant."); *In re Lulu*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984) ("The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound.").

Here, the prior art does not disclose any relevant cDNA molecules, let alone close relatives of the specific, structurally-defined cDNA molecules of claims 5 and 7 that might render them obvious. Maniatis suggests an allegedly obvious process for trying to isolate cDNA molecules, but that, as we will indicate below, does not fill the gap regarding the subject matter of claims 5 and 7. Further, while the general idea of the claimed molecules, their function, and their general chemical nature may have been obvious from Bohlen's teachings, and the knowledge that some gene existed may have been clear, the precise cDNA molecules of claims 5 and 7 would not have been obvious over the Bohlen reference because Bohlen teaches proteins, not the claimed or closely related cDNA molecules. The redundancy of the genetic code precluded contemplation of or focus on the specific cDNA molecules of claims 5 and 7. Thus, one could not have conceived the subject matter of claims 5 and 7 based on the teachings in the cited prior art because, until the claimed molecules were actually isolated and purified, it would have been highly unlikely for one of ordinary skill in the art to contemplate what was ultimately obtained. What cannot be contemplated or conceived cannot be obvious.

The PTO's theory that one might have been motivated to try to do what Deuel in fact accomplished amounts to speculation and an impermissible hindsight reconstruction of the claimed invention. It also ignores the fact that claims 5 and 7 are limited to specific compounds, and any motivation that existed was a general one, to try to obtain a gene that was yet undefined and may have constituted many forms. A general motivation to search for some gene that exists does not necessarily make obvious a specifically-defined gene that is subsequently obtained as a result of that search. More is needed and it is not found here.

The genetic code relationship between proteins and nucleic acids does not overcome the deficiencies of the cited references. A prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein. No particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate that it should be prepared. We recently held in *In re Baird*, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994), that a broad genus does not necessarily render obvious each compound within its scope. Similarly, knowledge of a protein does not give one a conception of a particular DNA encoding it. Thus, *a fortiori*, Bohlen's disclosure of the N-terminal portion of a protein, which the PTO urges is the same as HBGF, would not have suggested the particular cDNA molecules

defined by claims 5 and 7. This is so even though one skilled in the art knew that some DNA, albeit not in purified and isolated form, did exist. The compounds of claims 5 and 7 are specific compounds not suggested by the prior art. A different result might pertain, however, if there were prior art, *e.g.*, a protein of sufficiently small size and simplicity, so that lacking redundancy, each possible DNA would be obvious over the protein. See *In re Petering*, 301 F.2d 676 (CCPA 1962) (prior art reference disclosing limited genus of 20 compounds rendered every species within the genus unpatentable). That is not the case here.

The PTO's focus on known methods for potentially isolating the claimed DNA molecules is also misplaced because the claims at issue define compounds, not methods. See *In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993). In *Bell*, the PTO asserted a rejection based upon the combination of a primary reference disclosing a protein (*and its complete amino acid sequence*) with a secondary reference describing a general method of gene cloning. We reversed the rejection, holding in part that " [t]he PTO's focus on Bell's method is misplaced. Bell does not claim a method. Bell claims compositions, and the issue is the obviousness of the claimed compositions, not of the method by which they are made." *Id.*

We today reaffirm the principle, stated in *Bell*, that the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs. A prior art disclosure of a process *reciting a particular compound* or obvious variant thereof as a product of the process is, of course, another matter, raising issues of anticipation under 35 U.S.C. Section 102 as well as obviousness under Section 103. Moreover, where there is prior art that suggests a claimed compound, the existence, or lack thereof, of an enabling process for making that compound is surely a factor

Page 1216

in any patentability determination. See *In re Brown*, 329 F.2d 1006, 141 USPQ 245 (CCPA 1964) (reversing rejection for lack of an enabling method of making the claimed compound). There must, however, still be prior art that suggests the claimed compound in order for a *prima facie* case of obviousness to be made out; as we have already indicated, that prior art was lacking here with respect to claims 5 and 7. Thus, even if, as the examiner stated, the existence of general cloning techniques, coupled with knowledge of a protein's structure, might have provided motivation to prepare a cDNA or made it obvious to prepare a cDNA, that does not necessarily make obvious a particular claimed cDNA. "Obvious to try" has long been held not to constitute obviousness. *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. Thus, Maniatis's teachings, even in combination with Bohlen, fail to suggest the claimed invention.

The PTO argues that a compound may be defined by its process of preparation and therefore that a conceived process for making or isolating it provides a definition for it and can render it obvious. It cites *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016

(Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991), for that proposition. We disagree. The fact that one can conceive a general process in advance for preparing an *undefined* compound does not mean that a claimed *specific* compound was precisely envisioned and therefore obvious. A substance may indeed be defined by its process of preparation. That occurs, however, when it has already been prepared by that process and one therefore knows that the result of that process is the stated compound. The process is part of the definition of the compound. But that is not possible in advance, especially when the hypothetical process is only a general one. Thus, a conceived method of preparing some undefined DNA does not define it with the precision necessary to render it obvious over the protein it encodes. We did not state otherwise in *Amgen*. See *Amgen*, 927 F.2d at 1206-9, 18 USPQ2d at 1021-23 (isolated/purified human gene held nonobvious; no conception of gene without envisioning its precise identity despite conception of general process of preparation).

We conclude that, because the applied references do not teach or suggest the claimed cDNA molecules, the final rejection of claims 5 and 7 must be reversed. See also *Bell*, 991 F.2d at 784-85, 26 USPQ2d at 1531-32 (human DNA sequences encoding IGF proteins nonobvious over asserted combination of references showing gene cloning method and complete amino acid sequences of IGFs).

Claims 4 and 6 are of a different scope than claims 5 and 7. As is conceded by Deuel, they generically encompass all DNA sequences encoding human and bovine HBGFs. Written in such a result-oriented form, claims 4 and 6 are thus tantamount to the general idea of all genes encoding the protein, all solutions to the problem. Such an idea might have been obvious from the *complete* amino acid sequence of the protein, coupled with knowledge of the genetic code, because this information may have enabled a person of ordinary skill in the art to envision the idea of, and, perhaps with the aid of a computer, even identify all members of the claimed genus. The Bohlen reference, however, only discloses a partial amino acid sequence, and thus it appears that, based on the above analysis, the claimed genus would not have been obvious over this prior art disclosure. We will therefore also reverse the final rejection of claims 4 and 6 because neither the Board nor the patent examiner articulated any separate reasons for holding these claims unpatentable apart from the grounds discussed above.

One further matter requires comment. Because Deuel's patent application does not describe how to obtain any DNA except the disclosed cDNA molecules, claims 4 and 6 may be considered to be inadequately supported by the disclosure of the application. See generally *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.) (generic DNA sequence claims held invalid under 35 U.S.C. Section 112, first paragraph), *cert. denied*, 502 U.S. 856 (1991); *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (Section 112 "requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). As this issue is not before us, however, we will not address whether claims 4 and 6 satisfy the enablement requirement of Section 112, first paragraph, but will leave to the PTO the question whether any further rejection is appropriate.

We have considered the PTO's remaining arguments and find them not persuasive.

CONCLUSION

The Board's decision affirming the final rejection of claims 4-7 is reversed. *REVERSED*

Footnotes

Footnote 1. For a more extensive discussion of recombinant DNA technology, see *In re O'Farrell*, 853 F.2d 894, 895-99, 7 USPQ2d 1673, 1674-77 (Fed. Cir. 1988); *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991).

Footnote 2. Deuel determined that the N-terminal sequence of bovine uterus HBGF is Gly - Lys - Lys - Glu - Lys - Pro - Glu - Lys - Lys - Val - Lys - Lys - Ser - Asp - Cys - Gly - Glu - Trp - Gln - Trp - Ser - Val - Cys - Val - Pro.

Footnote 3. European Patent Application No. 0326075, naming Peter Bohlen as inventor, published August 2, 1989.

Footnote 4. Maniatis et al., *Molecular Cloning: A Laboratory Manual*, "Screening Bacteriophage [lambda] Libraries for Specific DNA Sequences by Recombination in *Escherichia coli*," Cold Spring Harbor Laboratory, New York, 1982, pp. 353-361.

Footnote 5. Bohlen's disclosed N-terminal sequence for human and bovine HBBMs is Gly - Lys - Lys - Glu - Lys - Pro - Glu - Lys - Lys - Val - Lys - Lys - Ser - Asp - Cys - Gly - Glu - Trp - Gln. This sequence matches the first 19 amino acids of Deuel's disclosed N-terminal sequence.

Footnote 6. The examiner and the Board apparently used the term "gene" to refer both to natural (chromosomal) DNA and synthetic cDNA. We will use the several terms as appropriate.

Footnote 7. Deuel is supported in its appeal by an *amicus curiae* brief submitted by the Biotechnology Industry Organization and the Bay Area Science Center. Amici urge that, contrary to controlling precedent, the PTO has unlawfully adopted a *per se* rule that a gene is *prima facie* obvious when at least part of the amino acid sequence of the protein encoded by the gene is known in the prior art.

- End of Case -